

EXHIBIT 1

Fractogel[®] EMD

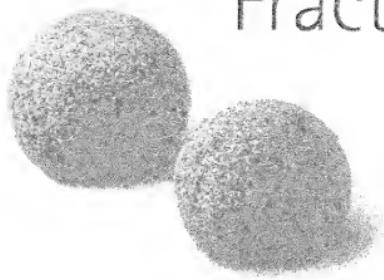
Process media

Life Science Products
Processing

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Fractogel[®] EMD Process media

Improves "Process Economics" in the Separation of Bio-Molecules

Specialists in the production of bio-molecules have been using Fractogel[®] EMD process media for more than 10 years. During the past decade an increasing number of downstream processes have been developed using semi-rigid Fractogel[®] EMD media in process chromatographic steps.

The high efficiency and economy of all Fractogel[®] EMD media are advantageous due to the strong binding of bio-molecules and the long life time of the material. Above all, Fractogel[®] EMD process media are used because of the excellent yield together with the high number of cycles over the life time of the product.

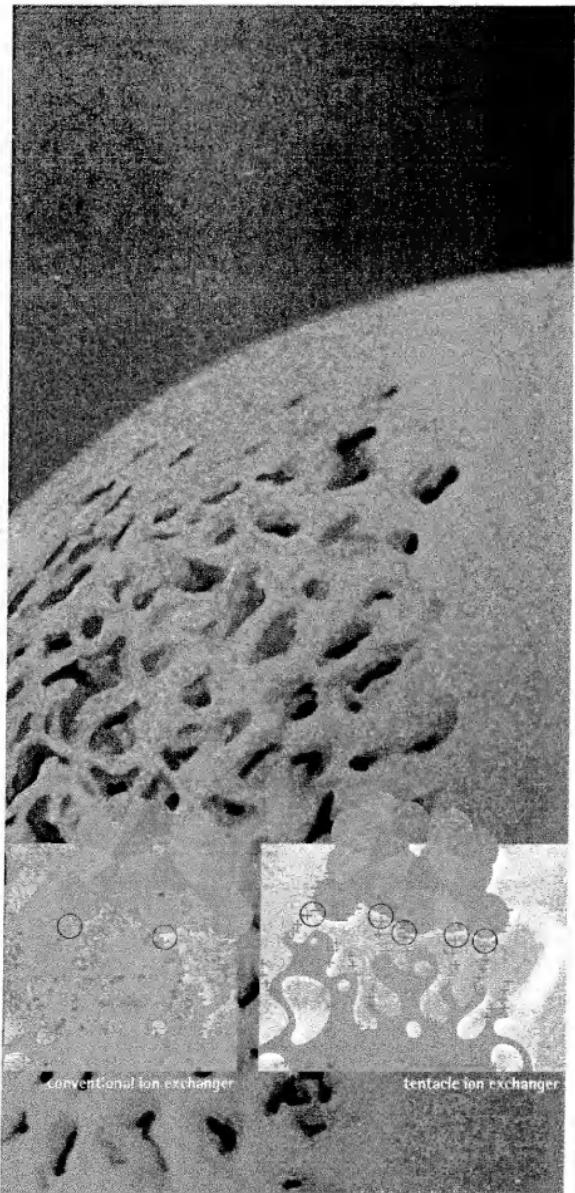
High capacity at high flow rates provides a powerful tool for the purification strategy especially if the target molecule is unstable. Saving time not only increases the yield but also improves process economics. Since the binding of bio-molecules is stronger with tentacle exchangers, a higher salt concentration in the sample will affect the binding capacity less compared to conventional gels. So Fractogel[®] EMD media provide more reliable results, flexibility of use and can be applied successfully to many and varied applications.

Above all, Fractogel[®] EMD media enables all those involved in Biopharmaceutical processing the use of a well tested production

tool. Compared to conventional resins Fractogel[®] EMD media improve the efficiency of the separation part of the production process.

Yields are higher, processes can be conducted at higher flow rates therefore reducing throughput time. Because the media lasts so long and can be used repeatedly, the economics of the process are very favourable.





What are Fractogel® EMD process media?

The Matrix

The structure of the Fractogel® particles is considerably different from that of other hydrophilic chromatographic resin like dextran, agarose or cellulose. Fractogel® is a synthetic methacrylate based polymeric resin providing an excellent pressure stability resulting in high flow rates. The process media consist of beads with a particle size between 40 and 100 µm. Fractogel® EMD BioSICU for size exclusion chromatography has a particle size in the range of 70–10 µm. The pores which are formed from inter-twisted polymer conglomerates have a size of about 800 Å enabling a free diffusion of proteins into the beads. The complete surface is strongly hydrophilic due to the ether linkages in the polymer.

The Tentacles

Long, linear polymer chains ("tentacles") carry the functional ligands. All tentacles are covalently attached to hydroxyl groups of the backbone structure of Fractogel®. Thus, both the bead and surface modification are stable to regeneration and sanitization. The main advantage of the tentacle chemistry is the large amount of sterically accessible ligands for the binding of biomolecules without any steric hindrance. Therefore, large biomolecules are much more tightly bound during the separation process. Different ligands are utilized for various application areas (ion exchange, affinity-, hydrophobic interaction chromatography).

Fractogel® EMD media application

Advantages of Fractogel® tentacle media

Better Production Yields

A result of the unique surface modification technique is the high binding capacity of all Fractogel® media. Due to the tighter binding of the target molecule, very often the capture step using Fractogel® ion exchange resins is more efficient than other resins. This more efficient capture results in greater overall yield than with other types of separation media.

Safer Product

In contrast to carbohydrate supports Fractogel® media are resistant to microbial degradation. Thus, the risk of contamination with endotoxins is greatly reduced. In addition the ability to clean Fractogel® media guarantees a long lifetime. This is an important feature especially when recombinant proteins, produced from micro-organisms, are purified.

Very Economical

Due to the chemical resistance of Fractogel® media a high number of cycles can be achieved. Therefore, resin lifetime is extremely long and replacement frequency is minimized resulting in lower operating costs.

Fig. 1:

Capacity at different flow rates.
Only with Fractogel® EMD tentacle
ion exchangers high capacities are
available at high flow rates.

High capacity at high flow rates

High yields, see stability

High chemical stability

Superior elution behavior

High recovery of bound proteins

Uniform particle size distribution

Efficient backwash, low backwash volume

Regulatory Standard like available

- high throughput
- high flow rates
- easy cleaning in place (CIP)
- efficient capture
- high yield
- good resolution
- high purity of the target molecule
- support for process validation

Matrix	crosslinked polymethacrylate
Properties of the tentacle Fractogel® EMD types:	
Particle Size	S-type: 20 - 40 µm M-type: 40 - 90 µm
Pore size	About 800 Å
pH stability range	pH 1 up to 13
Pressure limit	8 bar
Linear flow rate	Up to 260 cm/h (S-type), up to 800 cm/h (M-type)
Storage	150 mM NaCl, 20% ethanol
Regeneration	1-2 M NaCl for IEX, Chelate, TEA, BiOSEC except HIC
Sanitization	0.1 - 0.5 M NaOH

advantage

Application Areas

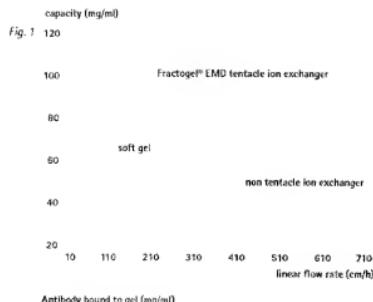
Rapid protein purification

The main application area of Fractogel® media is the isolation of proteins. Native or recombinant blood plasma factors are processed on Fractogel® EMD ion exchangers with high throughput rates. Peptides and low molecular weight substances (e. g. NAD⁺, ATP, gangliosides) can also be purified efficiently.

Recombinant His-tagged proteins can be purified on Fractogel® EMD Chelate.

Efficient protein polishing

Size exclusion chromatography (SEC) on Fractogel® EMD BioSEC can be used as an efficient polishing step of IgG, IgM, recombinant proteins, plasma factors and others.



High yield antibody isolation

In the case of antibody purification, samples can be loaded directly onto Fractogel® EMD SO₃⁻ (M) and/or Fractogel® EMD SE HiCap whereas serum albumin, nucleic acids, and Phenol Red will not bind. This can remove the need for preparation steps prior to purification. Fractogel® EMD TA is an affinity resin designed specifically for the purification of antibodies and can be utilised instead of ion exchangers or in combination with other methods. The functional group is a small, synthetic ligand, and unlike Protein A, antibodies can be eluted at physiological pH conditions.

Effective DNA removal

DNA removal during the preparation of homogeneous protein samples can be performed using tentacle anion exchange columns, where the DNA binds to the resin. Tentacle cation exchangers can be used to eliminate DNA in the flow-through mode. Small and large scale purification of plasmid DNA is performed on Fractogel® anion exchangers.

Improved virus separation

Fractogel® EMD anion exchangers were shown to be effective in removing a broad range of viruses from process streams. As the binding of virus to the resin was strong, protein could be separated from the contaminating viruses using different salt concentrations. Viral clearance for Fractogel® EMD TMAE and Fractogel® EMD DEAE are in the 5–6 log reduction range. However, it was shown that subsequent elution of virus from these resins in high salt, yielded a large fraction of viable virus enabling the users to calculate the balance of virus reduction. Loading and elution conditions were then investigated that led to the purification of virus on these resins. The use of Fractogel® EMD TMAE or DEAE for the purification of viruses is now replacing the more traditional methods of centrifugation and SIC. Thus, the production of virus particles as well as the removal of viral contamination can be achieved easily using tentacle resins.

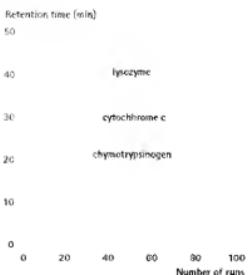
Fig. 2:

Binding of an antibody onto different cation exchangers at pH 6.5. With Fractogel® EMD tentacle ion exchangers high binding capacities can be utilized even at high salt concentrations. The buffer concentration is expressed as the sum of the molarities of sodium chloride and sodium phosphate

Fractogel® EMD media an excellent

Fig. 3:

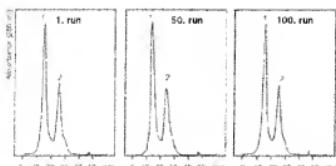
Reproducibility of 100 cycles on Fractogel® EMD S03-(M). The elution positions of the proteins remain the same for at least 100 runs.



High Stability – an excellent long term investment

Since the tentacles are very stable, the resins can be used for hundreds of cycles. Even long term treatment with 0.2 M NaOH for more than 8 months results in a loss of binding capacity of less than 10 % of the initial value. More importantly, no resin-derived compounds

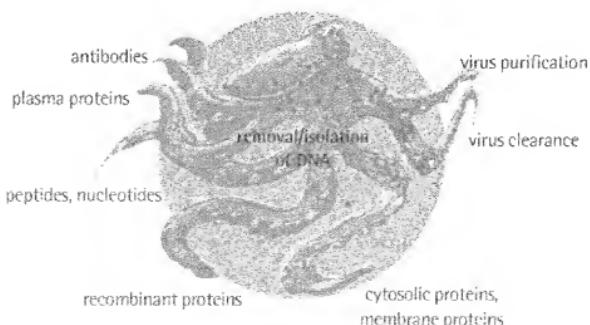
can be detected in the protein preparation after the recommended cleaning protocols are applied. The chromatographic performance characteristics are not changed after hundreds of purification and regeneration cycles. Corresponding data are summarised in the individual Regulatory Support Files documentation (RSF).



Application Areas

Fig. 4:

Chromatographic reproducibility after 100 repetitive injections onto Fractogel® EMD TMAE(M). Chromatograms from a Fractogel® EMD TMAE(M) column (S0-10) showing the separation of a test mixture containing conalbumin (peak 1) and human serum albumin (peak 2).



investment

Fractogel® EMD tentacle media

Ordering information

Description	Catalogue No.	Coordinates cm ²	Pore size μm	Capacity (estimated)	Type of chromatography
Fractogel® EMD media					
Fractogel® strong anion exchanger					
Fractogel® EMD TMAE (M)	3.14981	100, 500, 5000	40-90	100mg BSA	strong anion exchange chromatography
Fractogel® EMD TMAE (K) (M)	3.10276	100, 500, 5000	40-90	100mg BSA	strong anion exchange chromatography
Fractogel® EMD TMAE (S)	3.16982	100, 500*	20-40	100mg BSA	strong anion exchange chromatography
Fractogel® weak anion exchanger					
Fractogel® EMD DAE (M)	3.16970	100, 500, 5000	40-90	100mg BSA	weak anion exchange chromatography
Fractogel® EMD DAE (S)	3.16978	100, 500*	20-40	100mg BSA	weak anion exchange chromatography
Fractogel® EMD DMAE (M)	3.16954	100, 500, 5000	40-90	100mg BSA	weak anion exchange chromatography
Fractogel® EMD DMAE (S)	3.16969	100, 500*	20-40	100mg BSA	weak anion exchange chromatography
Fractogel® strong cation exchanger					
Fractogel® EMD SO ₃ ⁻ (M)	3.13872	100, 500, 5000	40-90	100mg Lys	strong cation exchange chromatography
Fractogel® EMD SO ₃ ⁻ (K) (M)	3.14994	100, 500, 5000	40-90	100mg Lys	strong cation exchange chromatography
Fractogel® EMD SO ₃ ⁻ (S)	3.16960	100, 500*	20-40	100mg Lys	strong cation exchange chromatography
Fractogel® weak cation exchanger					
Fractogel® EMD COO ⁻ (M)	3.13895	100, 500, 5000	40-90	100mg Lys	weak cation exchange chromatography
Fractogel® EMD COO ⁻ (S)	3.16997	100, 500*	20-40	100mg Lys	weak cation exchange chromatography
Fractogel® SEC media					
Fractogel® EMD BioSEC	1.10117	150, 1000, 5000	20-40	5-1000 kDa	Size exclusion chromatography
Fractogel® affinity media					
Fractogel® EMD Osteo (M)	3.10738	250, 500, 5000	40-90	80 μmol Cu	metal affinity chromatography
Fractogel® EMD Amino (M)	3.14893	500, 5000	40-90	40 μmol	affinity chromatography
Fractogel® EMD TA (S)	3.16473	25, 250	20-40	25 mg IgG	affinity chromatography
Fractogel® activated media					
Fractogel® EMD Epoxy (M)	3.16961	10g, 100g	40-90	1.5mm ² /g	activated surface chromatography
Fractogel® HIC media					
Fractogel® EMD Propyl 800 (S)	3.10965	100, 500*	20-40	25mg Ovab.	weak HIC
Fractogel® EMD Propyl 800 (M)	3.16197	100, 500*	20-40	25mg Ovab.	weak HIC
Fractogel® EMD Phenyl 800 (M)					strong HIC

* larger quantities on request.

FDA Registration numbers of Fractogel® media

Product	Cat. No.	Reg. M.F.C.
Fractogel® EMD TMAE S, M, K, (S)	1000, 10000, 100000	5145
Fractogel® EMD TA S, M, (S)	1000, 10000	5004
Fractogel® EMD COO S, M, (S)	5000, 10000	4707
Fractogel® EMD COO S, M, (K) (S)	1000, 10000	7193
Fractogel® EMD BioSEC S, M	10, 100	9114
Fractogel® EMD Osteo S, M	1000, 10000	5002
Fractogel® EMD Phenyl 800 S, M	1000, 10000	5228

Selected papers:

B.G. Huygen et al., Purification of IgG by Recombinant Adenovirus Encoding Human p35 by Coupling to a Tentacle Matrix, *Human Gene Therapy* 6 (1995) 1409-1416.

C. Pich et al., Process Development for the Manufacture of Inactivated HIV-1, *Biopharm. &.* 4 (1995) 28-35.

M. Gottschalk et al., Preparative capturing of mouse monoclonal antibodies from cell culture supernatant by cation exchange chromatography, *Sieg Wiss.* 3 (1991) 42-44.

D. Jönig et al., Size-exclusion chromatography of plasma proteins with high resolution matrices, *J. Chromatogr.* 799 (1996) 205-214.

D. Hoffmann et al., Large scale purification of oligopeptides GM3 (Neu5Gc) and GM3 (Neu5GC) by trimethylaminomethyl Fractogel® high performance liquid chromatography, *J. Chromatogr.* B 710 (1998) 1-8.

J.K. Waller et al., Virus Removal and Inactivation, ACS Symp. Series 630: Validation of Biopharmaceutical Manufacturing Processes, Am. Chem. Soc. (1996) 114-125.

J.K. Waller, T. Nohlfelder, W. Weiz, Validation of Viral Safety for Enzymatic Cell Detoxification, Protein Separation and Purification, 11. Symposium für Virologie, 27.9.-29.9.1998, Göttingen, pp. 704-709.



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